Quantification of Myocardial Perfusion and Function

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Quantification of Myocardial Perfusion

Data-based methods for identifying in patients myocardial perfusion abnormalities from Tl-201 SPECT studies have been previously developed and commercialized by investigators at Cedars-Sinai Medical Center[1] and Emory University[2] and reported as early as 1985. These methods utilized a statistically defined data base of normal patients to be used as a pattern to compare prospective CAD patients. Although these methods have been extensively validated[2-4] and proven to be clinically valuable[5] in standardizing and objectifying myocardial perfusion scans they have been limited by several deficiencies.

Five major limitations have been identified with these early approaches. One limitation has been the extensive operator interaction. This results in a reduced objectivity and reproducibility of the program. By automating this process this limitation has been overcome as has been partially addressed in the previous section. A second limitation has been the failure to sample the count distribution perpendicular to the myocardial wall particularly at the apex. This usually results in artifactually increasing the counts from the apical region. A third limitation has been the lack of data-bases for perfusion tracers other than Tl-201. Comparison of patients acquired with different tracers and or different protocols to the Tl-201 data base often leads to incorrect identification of abnormalities. A fourth limitation has been the inability of these data-based approaches to compensate for attenuation in a patient whose attenuating tissue (such as breast and diaphragm) is significantly more than those of the normal patients selected for the normal data base. This almost always leads to artifactually defining these photopenic regions as hypoperfused myocardium. The fifth limitation has been the inability of the polar map display to accurately represent the true extent and location of an abnormality. This is due to the warping created by transforming a three-dimensional distribution onto a two dimensional polar map. This limitation results in underestimating the extent of hypoperfused apical regions and overestimating the extent of hypoperfused basal regions.

More recently, investigators working at Emory University and Cedars-Sinai Medical Center have developed[6] and extensively validated[7] a new data-based quantitative package known as CEqual-R (Cedars-Emory Quantitative Analysis) designed to overcome the above-mentioned limitations. The attributes of this approach are described below.

Methods

This quantitative method uses several image identification techniques (e.g. image clustering, filtered thresholding, and specified threshold con-

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straints) for isolation of the left myocardium from the remainder of the image.[8] Once the left myocardium is identified, the apical and basal image slices, the (x, y) coordinates of the central axis of the ventricular chamber, and a limiting radius for the maximum count circumferential profile search are determined automatically. In the majority of cases, operator interaction is required only for verification of automatically determined parameters. If at any time the program fails to locate any of the features, it will branch to an interactive mode and require the operator to select the parameters manually.

The CEqual technique has been developed to generate count profiles from a hybrid, two-part, three-dimensional sampling scheme of stacked short-axis slices. In this approach the apical region of the myocardium is sampled using spherical coordinates, and the rest of the myocardium is sampled using cylindrical coordinates. This approach promotes a radial sampling which is mostly perpendicular to the myocardial wall for all points and thus results in a more accurate representation of the perfusion distribution with minimal missampling effects. Following operator verification of the automatically derived features, the three dimensional maximum count myocardial distribution is extracted from all stacked short axis tomograms. Maximum count circumferential profiles, each comprised of 40 points, are automatically generated from the short-axis slices using this 2-part sampling scheme. These profiles are generated for the stress and rest myocardial perfusion distributions. A normalized percent change between stress and rest is also calculated as a reversibility circumferential profile. The most normal region of the stress distribution is used for normalizing the rest to the stress distribution.

Multi-Dimensional Displays of Myocardial Perfusion

1. Polar Map Displays

Polar maps, sometimes called bull's-eye displays, are the standard for viewing myocardial perfusion distributions.[1,2] These give a quick and comprehensive overview of the circumferential samples from all slices by combining these into a color-coded display. The extracted counts from myocardial sampled points are assigned a color based on normalized coint values, and the colored profiles are shaped into concentric rings. The most apical slice processed forms the center of the polar map, and each successive profile from each successive slice is displayed as a new ring surrounding the previous. The most basal slice of the left ventricle makes up the outermost ring of the polar map.

The use of color helps identify abnormal areas at a glance. Abnormal regions from the stress study can be assigned a black color, thus creating a blackout map. Blacked-out areas that normalize at rest are color-coded white, thus creating a whiteout reversiblity map.[9] Additional maps such as a standard deviation map that shows the number of standard deviations below normal of each point in each circumferential profile, can aid in evaluation of the study by indicating the severity of the abnormality.

Polar maps while offering a comprehensive view of the quantitative results, distort the size and shape of the myocardium and any defects. Two new polar maps have been developed for displaying more accurately the extracted three-dimensional tracer distribution. The first one, called distance-weighted, represents the counts from each sample in color-coded elements of equal width from apex to base. These maps have been shown

to be useful for accurate localization of abnormalities. The second one, called volume-weighted, represents the counts from each sample in color-coded elements in such a way that the area of each displayed polar ring is proportional to the volume of the corresponding myocardial slice. This type of map has been shown to be best for estimating defect size. However, more realistic displays have been introduced which do not suffer from the distortions of polar maps.

2. Three Dimensional Displays

We have also been investigating the use of three-dimensional surface renderings to represent the myocardial perfusion distribution.[10] In this approach the 3-D Cartesian coordinates of the maximal count pixels from where the samples have been extracted are used to render the 3-D surface of the myocardium. Each point in the myocardial surface is color-coded according to the count density at that location and shaded according to the angle that an imaginary light source makes with the surface and the observer frame of reference. Optimal rendering requires the use of 24 bits per pixel in order to generate a display to the eye which truly appears three-dimensional.

3. New Data Bases

Using the CEqual approach normal limits were defined from a group of patients with less than 5% probability of coronary artery disease. Gender matched normal data bases have been defined[11] and validated for the following SPECT protocols: 1. Low dose rest, high dose stress, one-day Tc-99m sestamibi (Cardiolite) protocol;[7] 2. High dose stress and rest two-day Tc-99m sestamibi protocol; 3. Stress-redistribution Tl-201 protocol, 4. Rest Tl-201/stress Tc-99m sestamibi dual isotope protocol[12] and 5. Low dose stress, high dose rest Tc-99m Tetrofosmin (Myoview) one day protocol. All protocols used treadmill exercise to stress the patients.

For each of these protocols the normal data base, criteria for abnormality and prospective validation were performed in a standardized approach.[11] From the low likelihood patients the normal mean and standard deviation for each myocardial sample was determined. From expert visual interpretation of normal and hypoperfused regions the objective criteria for abnormality was determined. This criteria is based on how many standard deviations below the mean normal distribution constitute an abnormality for each myocardial wall. This is necessary to be established since these normal count distributions are not distributed in a Gaussian or Bell-shaped curve distribution. Once the normal data base and criteria for abnormality are determined these are tested using a prospective patient population who has undergone coronary catheterization. Using angiography as a gold-standard the accuracy of the method and protocols are established.

The choice of which radiopharmaceutical and/or protocol should be used is more of a clinical question or a question of laboratory logistics and are beyond the scope of this chapter. There are a number of questions related to these normal data bases which are very often asked and which merit further discussion.

One concern is whether the normal data bases developed using patients stressed with exercise can be used for patients undergoing pharmacological stress. It is evident by looking at these studies that patients imaged after pharmacological stress have more background activity and more myocardial activity than patients undergoing treadmill exercise. Nevertheless, the relative distribution in normal and CAD patients are similar enough that when the same normal data base is used for both forms of stress it results in similar diagnostic accuracy.[13]

Although it would be ideal to have separate data bases for protocols using pharmacological stress the development cost would be prohibitive.

A second concern is whether the normal data base developed for Tl-201 stress/redistribution studies may be used for stress/reinjection protocols. The stress protocol is the same for both studies and thus no new errors should be introduced. The reinjection images do appear different than the redistribution images. Nevertheless, in the CEqual program the resting distribution is not quantified but rather the reversibility or change between rest and stress. Since reinjection is supposed to result in a more marked difference between the two physiological states it is actually easier for the program to detect this difference in the form of defect reversibility. Thus the stress/redistribution Tl-201 normal data base may be used to quantify stress/reinjection studies.

The last concern is whether the normal data base for the Tc-99m sestamibi protocols may be used for Tc-99m tetrofosmin studies and vice-versa. Although there are some subtle differences as to how these two radiopharmaceuticals are distributed in the body the main parameters driving the final count distributions in the images are the type of collimators and filters used for a given count distribution. It does appear that these normal data bases are interchangable but additional studies are required to confirm these observations.

Compensation for Physical Effects and Implication on Quantification

Algorithms for compensating for photon attenuation, scatter and collimation effects in SPECT imaging have been developed over the last 20 years and are well understood.[14-16] Although these compensations are not exact analytic corrections, like in PET imaging, preliminary results indicate that their use should improve myocardial perfusion images.[17]

It is expected that these improvements will result in increased accuracy for detecting coronary artery disease, particularly in improving specificity through correction of diaphragmatic and breast attenuation artifacts. The application of these compensations will result in a concomitant shift in the normal myocardial tracer distribution previously learned by experts which could have a temporary confounding effect. Moreover, since the accuracy is already high for diagnosing CAD by experts who have learned to read around these artifacts from the non-compensated studies, it is expected that these compensations will help most those with a more limited expertise.

Commercial implementations of these compensations vary somewhat between manufacturers. The main differences are related to: a) the geometry (parallel vs. converging) of how the transmission and emission images are generated, b) the degree, if any, to which the algorithms compensate for attenuation, scatter and collimation effects, and c) the exact mathematical formulation of the algorithms used to reconstruct and correct the images. It is of concern that variations in the actual implementations of these compensations could create variations in the expected normal tracer distribution between systems by different manufacturers or between patients with different anatomy. These variants can complicate image interpretation and comparison to a normal data base. Large, prospective clinical trials are needed to document the advantages and limitations of the different approaches. It is expected that as more data becomes available, manufacturers will drift to a common approach for image compensation thus facilitating visual interpretation and image quantification.

Functional Assessment from Gated Myocardial Perfusion SPECT Studies

1. Multiple-gated SPECT

Many commercial nuclear medicine computer systems now have the capability of acquiring and reconstructing multiple-gated tomographic studies. This feature has promoted studies investigating the use of SPECT for assessing cardiac global and regional function, including the assessment of myocardial wall thickening. These assessments have been primarily investigated using Tc-99m red blood cells blood pool tomographic imaging,[18] and by using tomographic imaging of the Tc-99m Sestamibi perfused myocardial wall.[19]

2. Acquisition and Reconstruction

Acquisition consists of performing multiple gated acquisition at each of the planar projections for the same total time per projection. These acquisitions are usually obtained at one minute or less per projection so as to maintain the total study time to within 30 minutes to an hour. Because of both the short acquisition per projection and the consideration of reconstruction times, the number of frames per cardiac cycle are kept to a minimum, i.e., between 8 and 16. The reconstruction process is the same as that of non-gated SPECT except that each of the frames per cardiac cycle have to be shuffled so that individual projection sets are created for each frame of the cardiac cycle. Thus if, for example, a multiple-gated SPECT study is acquired at 8 frames per cardiac cycle, 8 individual sets of projections are created, and subsequently individually reconstructed. Once reconstructed into transaxial slices, each set is reconstructed along the same oblique angles in order to generate vertical, horizontal and short axis slices that have the same orientation from frame to frame. Once these oblique slices are generated the program reshuffles back each of the slices from each of the 8 individual tomographic sets into sets of 8 frames, multiple-gated tomographic slices which may be displayed in a closed-loop cine format for assessment of cardiac function. This same procedure is performed for either blood pool imaging or for imaging of the perfused myocardial walls.

3. Tc-99m Sestamibi

The exercise study is ECG-gated using 8 frames for the cardiac cycle. We have noted that cine diplay of the myocardial Sestamibi distribution throughout the cardiac cycle has been useful in identifying imaging artifacts. This type of display has also been shown to assist in assessing wall motion and thickening useful in determining myocardial viability. Assessment of myocardial thickening uses the fact[20] that objects such as myocardial walls smaller than two spatial resolution distances in thickness (~26 mm) exhibit a maximal count which is proportional to the thickness of the object. Thus visual assessment consists of determining if each region of the myocardium brightens as the myocardium thickens at end-systole. Relative quantification of myocardial thickening uses a count-based method consisting of determining the count change from end-systole to end-diastole. The spatial resolution of SPECT is too low to actually measure absolute thickness. Quantification of regional perfusion uses the combined counts from all 8 frames.

4. Clinical Applications

Gated SPECT of myocardial perfusion distributions has already been found to be useful clinically to characterize fixed myocardial defects as infarct or artifact.[21] The specificity of the method is enhanced by avoiding attenuation artifacts by

recognizing that myocardial walls with fixed defects that thicken (get brighter) during contraction must not be associated with infarcts. This count increase has also been validated to agree with wall thickening as assessed by 2D echocardiography.[22] Moreover, in patients with no previous myocardial infarction, it has been shown that a single gated stress perfusion study can replace the conventional rest-stress protocol since the resting myocardial thickening distribution is predictive of both the resting perfusion distribution and thus myocardial viability.[22]

Gated myocardial perfusion SPECT has also been shown to be useful in the measurement of resting LVEF either through the use of manual[23] or totally automatic methods.[24] This methodology has also been shown to have the potential for measuring myocardial thickening.[25] Many of these methods have been commercialized under the following names: Emory Cardiac Toolbox , QGS, 3-D MSPECT, SPECTEF and Multidim. Many of these commercial implementations measure volumes, mass, TID and heart/lung ratio.

Suggested Reading

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